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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application N.	Applicant(s)	
	09/927,597	MALIK ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Peri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1-7 and 11-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8 and 9* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

nt(s)

ce of References Cited (PTO-892)

ce of Draftsperson's Patent Drawing Review (PTO-948)

nation Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .

4)☐ Interview Summary (PTO-413) Paper No(s). _____ .

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other: .

DETAILED ACTION

Status of the Application

[1] Claims 1-15 are pending in the application.

[2] References A-K of the information disclosure statement of Paper No. 4 have been considered. Because information disclosed at internet web sites is subject to change, the hyperlinks for references G and K have been lined through.

Election/Restriction

[3] Applicant's election with traverse of Group III, claims 8-10 in Paper No. 8, filed August 04, 2003, is acknowledged. Applicant traverses the restriction by arguing (beginning at the top of page 2 of Paper No. 8) that claims 8-10 should not be restricted to two groups (Groups III and IV) because: 1) claims cannot be restricted without a showing that a search and examination of the claims would constitute an undue burden even when claims are directed to independent and distinct inventions because SEQ ID NO:2 and 4 are similar and share much of the same sequence and 2) it is the Office's policy to consider 10 amino acid sequences, even if the sequences are independent and distinct. Applicant's arguments are not found persuasive.

Regarding the substantial similarity of SEQ ID NO:2 and 4, a sequence alignment of SEQ ID NO:2 and SEQ ID NO:4 shows that, while the sequences are identical from amino acids 1 to 1936, the remaining C-terminal portions of each protein are *completely different* (see attached sequence comparison). Because each of the polypeptides is structurally distinct, the search for the polypeptide of SEQ ID NO:2 requires a search where no pertinent art to SEQ ID NO:4 exists, and vice versa. Therefore, a different field of search is required to search for each of the structurally distinct polypeptides of SEQ ID NO:2 and 4, resulting in an undue burden on the examiner. Regarding applicant's argument citing MPEP § 803.04, it is noted that this section of MPEP specifically addresses nucleic acid sequences and not amino acid sequences. Furthermore, this section of the MPEP states, "in most cases, *up to ten* independent and distinct nucleotide sequences will be examined in a single application without

restriction" (italics added for emphasis). Up to ten includes any number from one to ten. In the instant case, the examiner is co-examining six sequences, i.e., SEQ ID NO:2, 6, 8, 10, 12, and 14. This number properly lies within the "*up to ten*" number of sequences without restriction and, as stated above, to co-examine SEQ ID NO:4 with these six sequences would constitute an undue burden on the examiner.

Applicant further argues the claims of Groups V and VI should be rejoined with the product claims of Groups III and IV according to MPEP § 821.04. To the extent applicant's argument addresses rejoinder of the claims of Groups IV and VI, as co-examination of Group IV with elected Group III would constitute an undue burden on the examiner, Group IV will not be examined with the claims of the elected group and thus, rejoinder of the claims of Groups IV and VI is not required. Addressing rejoinder of the claims of Groups III and V, as the claims of Group III are not yet allowable, and rejoinder is not as yet required. If the polypeptide of Group III is found to be allowable, the claims of Group V will then be evaluated for rejoinder according to MPEP § 821.04.

[4] Claims 1-7 and 11-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

[5] Claims 8-10 are being examined on the merits only to the extent the claims read on the elected subject matter.

Claim Objections

[6] Claims 8-10 are objected to as reciting or being dependent upon claims that recite non-elected subject matter. It is suggested that, for example, applicant amend the claims such that they no longer recite non-elected subject matter.

[7] Claim 8 is objected to because of the recitation of "hSMMyHC". Abbreviations, unless otherwise well known in the art, should not be recited in the claims without at least once reciting the entire phrase, i.e., "human smooth muscle myosin heavy chain" for which the abbreviation is used. Appropriate correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[8] Claims 8-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention.

Claim 8 is drawn to a genus of isolated polypeptides having greater than 90% sequence identity to SEQ ID NO:2, 6, 8, 10, 12, and 14. Claim 9 limits the polypeptide of claim 8 to specifically binding to polyclonal antibodies generated against a protein comprising SEQ ID NO:2, 6, 8, 10, 12, and 14.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single representative species of the genus of claimed polypeptides, i.e., the polypeptide of SEQ ID NO:2 and fragments thereof (SEQ ID NO:6, 8, 10, 12, and 14). The specification fails to describe any additional representative species of the claimed genus. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an

unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". In the instant case, the claimed genus of polypeptides encompasses species that are widely variant in both structure and function, including (but not limited to) proteins having function other than ATPase activity and actin binding activity and non-functional polypeptides. As such, the disclosure of the single representative species of SEQ ID NO:2 is insufficient to be representative of the attributes and features of *all* species encompassed by the claimed genus of polypeptides. Given the lack of description of a representative number of polypeptides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[9] Claims 8-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO:2, 6, 8, 10, 12, and 14 and optionally wherein the polypeptide specifically binds to polyclonal antibodies generated against a polypeptide consisting of SEQ ID NO:2, 6, 8, 10, 12, or 14, does not reasonably provide enablement for the broad scope of claimed polypeptides, including *all* polypeptides having greater than 90% identity to SEQ ID NO:2, 6, 8, 10, 12, and 14 and optionally wherein the polypeptide specifically binds to polyclonal antibodies generated against a polypeptide *comprising* SEQ ID NO:2, 6, 8, 10, 12, or 14. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based

on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

- The claims are overly broad in scope: The claims are so broad as to encompass *all* polypeptides having greater than 90% identity to SEQ ID NO:2, 6, 8, 10, 12, and 14 and optionally wherein the polypeptide specifically binds to polyclonal antibodies generated against a polypeptide *comprising* SEQ ID NO:2, 6, 8, 10, 12, or 14 including polypeptides having function other than ATPase activity and actin binding activity and non-functional polypeptides. The broad scope of claimed polypeptides is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. In this case the disclosure is limited to the polypeptide of SEQ ID NO:2, 6, 8, 10, 12, and 14 and optionally wherein the polypeptide specifically binds to polyclonal antibodies generated against a polypeptide consisting of SEQ ID NO:2, 6, 8, 10, 12, or 14.

- The lack of guidance and working examples: The specification provides only a single working example of the claimed polypeptide, i.e., SEQ ID NO:2 and fragments thereof (SEQ ID NO:6, 8, 10, 12, and 14). This single working example fails to provide the necessary guidance for making and using the entire scope of claimed polypeptides. The specification fails to provide guidance regarding those amino acids of SEQ ID NO:2 that may be altered by substitution, addition, insertion, and/or deletion with an expectation of maintaining a desired activity. Furthermore, the specification fails to provide guidance as to how to use those variant polypeptides – both naturally and non-naturally occurring - that have activities other than ATPase or actin binding activity, e.g., non-functional polypeptides or polypeptides having activity other than ATPase or actin binding activity.

- The high degree of unpredictability in the art: The amino acid sequence of a polypeptide determines a protein's function. Predictability of which changes can be tolerated in a protein's amino acid sequence and obtain a desired activity requires a knowledge of and guidance with regard to which amino

acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within an amino acid sequence where modifications can be made with a reasonable expectation of success in obtaining a polypeptide having a desired activity are limited and the result of such modification(s) is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. In this case, the necessary guidance has *not* been provided in the specification as explained in detail above. Thus, in view of the lack of guidance regarding those amino acids that are necessary for the activity of the polypeptide of SEQ ID NO:2, 6, 8, 10, 12, and 14, a skilled artisan would recognize the high degree of unpredictability in altering the amino acid of SEQ ID NO:2, 6, 8, 10, 12, and 14 to obtain a polypeptide having a desired activity.

- The state of the prior art supports the high degree of unpredictability: The state of the art provides evidence for the high degree of unpredictability in altering the sequence of a polypeptide with an expectation that the polypeptide will maintain a desired activity/utility. For example, Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York, 1991) teach "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). While it is acknowledged that this reference was published in 1991, to date there remains no certain method for predicting the effects of even a *single* amino acid mutation on a protein. Such mutations may even completely alter a protein's activity. As a representative example, Witkowski et al. (*Biochemistry* 38:11643-11650) teach that a single amino acid substitution results in conversion of the parent polypeptide's activity from a beta-ketoacyl synthase to a malonyl decarboxylase (see e.g., Table 1, page 11647). Thus, the prior art acknowledges the unpredictability of altering a protein-encoding sequence

with an expectation of obtaining a protein having a desired function and discloses that even a single substitution in a polypeptide's amino acid sequence may completely alter the function of a polypeptide.

- The amount of experimentation required is undue: While methods of generating variants and homologues of a given polypeptide are known, it is not routine in the art to screen for *all* polypeptides having a substantial number of substitutions or modifications and having *any* function, as encompassed by the instant claims. Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[10] It is noted that SEQ ID NO:6, 8, 10, 12, and 14 are N-terminal fragments of the polypeptide of SEQ ID NO:2, SEQ ID NO:6 being the smallest fragment (see pages 7-8 of the specification). If the prior

art neither teaches or suggests a polypeptide of claims 8 and 9 reciting SEQ ID NO:6, the prior art would neither teach or suggest a polypeptide of claims 8 and 9 reciting SEQ ID NO:2, 8, 10, 12, or 14 as well. Thus, a prior art search has been conducted *only* for SEQ ID NO:6.

[11] Claims 8-9 are rejected under 35 U.S.C. 102(a) as being anticipated by Database GenPept Accession Number P35749 (gi:13432177). Claim 8 is drawn to an isolated polypeptide having greater than 90% sequence identity to SEQ ID NO:2, 6, 8, 10, 12, or 14. Claim 9 limits the polypeptide of claim 8 to specifically binding to polyclonal antibodies generated against a protein comprising SEQ ID NO:2, 6, 8, 10, 12, or 14. Database GenPept Accession Number P35749 teaches a polypeptide that is 98.5% identical to SEQ ID NO:6. This anticipates claims 8-9 as written.

[12] Claims 8-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Database GenPept Accession Number A41604 (gi:109322). Claims 8 and 9 are drawn to an isolated polypeptide as described above. Database GenPept Accession Number A41604 teaches a polypeptide that is 97.6% identical to SEQ ID NO:6. This anticipates claims 8-9 as written.

[13] Claims 8-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Database GenBank Accession Number AB020673 (gi:4240220). Claims 8 and 9 are drawn to an isolated polypeptide as described above. Database GenBank Accession Number AB020673 teaches a polypeptide that is 98.6% identical to SEQ ID NO:6. This anticipates claims 8-9 as written.

Conclusion

[14] Status of the claims:

- Claims 1-15 are pending.
- Claims 1-7 and 11-15 are withdrawn from consideration.
- Claims 8 and 9 are rejected.
- Claim 10 is objected to.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (703) 746-5078. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman
Patent Examiner
Art Unit 1652

09/22/03